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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | | ATTORNEY DOCKET NO. |
|---|---|---|---|---|
| 09/488,491 | 01/20/00 | LEVESQUE | M | CEDAR 042638 |

HM22/0814

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| EXAMINER | |
|---|---|
| SCHMIDT, M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1635 | 13 |

**DATE MAILED:** 08/14/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Offic Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/488,491 | LEVESQUE ET AL. | |
| | Examiner | Art Unit | |
| | Mary Schmidt | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-48 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

1. Claims 1-48 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Double Patenting*

3. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,087,168. Although the conflicting claims are not identical, they are not patentably distinct from each other for the same reasons of record as set forth in the Official Action mailed 11/22/00.

It is noted that Applicant will file a terminal disclaimer upon indication of allowable subject matter.

### *Claim Rejections - 35 USC § 112*

4. Claims 17-39 and 43-48 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the Official Action mailed 11/22/00.

Applicant's arguments filed 05/25/01 (which reference the remarks in the unentered amendment filed 03/26/01) have been fully considered but they are not persuasive.

Applicant notes that the summary of what the specification teaches is incorrect. It appears that this paragraph was inadvertently addressing the specification of the parent application, 09/234,332. The instant specification teaches the same methods for transdifferentiating epidermal cells into neuronal-like cells, except has the added features of antagonism of BMP. It is noted that the Figures and the Table teach that the addition of the BMP antagonist and the antisense oligonucleotides to the epidermal cells were able to produce cells which express Neurofilament M, a neuronal marker.

However, the rejection stands for the scope of such transdifferentiated cells claimed. As argued previously, one skilled in the art would not have been in possession of a representative number of species of such transdifferentiated cells from the teachings of the specification. The specification teaches that may possible outcomes are possible for neuronal type cells exposed to various growth factors and neurotransmitters for instance (see page 5, lines 14-29). It is precisely this variability that creates a broad genus of possible "neuronal-like" cells. The novel feature of the claimed invention is the addition of the antisense oligonucleotides to specific genes in addition to the well-known neural growth factors, which allows the epidermal basal cells to show specific physiological characteristics of a neuronal cell. However, one skilled in the art would not expect such a cell to have all the features of a neuronal cell, nor resemble a neuronal cell which developed naturally in the body since the artificial conditions creates a unique set of gene

expression. Thus the scope of possible slight modifications to such a cell is so large that the examples in the specification do not provide a representative number of the possible neuronal-type cells. As such, the claims lack written description as broadly claimed to cells having any possible physiological feature of a neuronal cell.

5. Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for differentiated cells showing some specific neuronal cell features, does not reasonably provide enablement for the scope of methods for making neuronal cells as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons of record as set forth in the Official Action mailed 11/22/00.

Applicant's arguments filed 05/25/01 (which reference the remarks in the unentered amendment filed 03/26/01) have been fully considered but they are not persuasive.

Applicant argues that (1) the specification teaches the source of the epidermal basal cells, (2) that the method serves to transdifferentiate a large subset of the cell population, and (3) that the Examiner's arguments concern practice of the claimed methods in whole organisms do not pertain to the *in vitro* methods of screening.

In response, the specification as filed teaches on page 14, lines 6-9, that the invention considers administration of the transdifferentiated cells to whole organisms and that once in a whole organism the "plasticity" of the cells would allow the cells to maintain neuronal

differentiation " in vitro or in situ, when implanted into the mammalian subject, without the further addition of antisense oligonucleotides." As such, the claims were broadly interpreted to allow for the "detecting the presence or absence of an effect of the potential nerve growth factor" (claim 40 for example) in whole organisms. In other words, wherein the cells are screened in vivo after transdifferentiation in vitro. Thus the arguments center on the unpredictability of the use of such cells in whole organisms.

The assertion that the specification teaches differentiation of a large subset of the cell population is not questioned, nor is the method for preparing the skin cells for transdifferentiation. The unpredictability in the claims centers on the scope of transdifferentiated cells claimed. As argued above and previously, the scope of the claims reads on making cells having any possible feature of a neuronal cell. Yet the specification as filed teaches specific physiological markers which identify the "transdifferentiated cells" in combination with the methods for making such cells as the novel invention claimed. The specification does not enable one skilled in the art to make and use cells having any possible neuronal feature via the claimed method for the following reasons: (1) the administration of the antisense to specific genes, and the growth of the cells in a specific media form a subset of cells having a specific physiology which differs from other neuronal cells which naturally develop in a whole organism; (2) as the specification teaches, there is a high level of diversity possible in neuronal growth based on the intricacies of numerous factors in the cell in response to the environmental stimuli of the cells. This variability produces a level of unpredictability in production of any transdifferentiated neuronal cell not enabled by the

specification as filed. Hence, the argument that it would take "trial and error" experimentation to make and use the claimed invention primarily centers on the idea that one skilled in the art would not know how to make and use any possible "transdifferentiated cell" with any possible combination of known neuronal growth factors, for instance, as broadly claimed.

Further, one would not expect that a cell having any one feature of a neuronal cell would act to function as a wild type neuronal cell for the purposes of screening for any drug target. The nexus between expression patterns of the claimed "transdifferentiated" cells and the expression patterns of a wild type neuronal cell in a whole organism upon administration of said drug are not known. For instance, in claim 42, how would one of skill in the art know that the transdifferentiated cells from a patient having any neuronal disorder, when exposed to a drug, would act as a model for treating said patient? Even though the cells come from the same patient, the transdifferentiation process enables a specific expression pattern which may or may not provide a reasonable model for the effects of a drug on the patient's neuronal cells. Further, which neuronal cells would the drug alter in the whole organism when administered? As such, the claims are broadly drawn to a scope of cells which is not enabled as written. While specific assay techniques are known in the art for detecting the effects of chemotherpeutic agents (or novel growth factors) as argued on page 15 of the response, it is not clear how the use of such assays would correlate to the use of the potential agent on cells in whole organisms. As such, one skilled in the art would necessarily practice undue experimentation to make and use the claimed methods of screening.

Applicant's arguments have not overcome the *prima facie* lack of enablement.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
August 12, 2001

ANDREW WANG
PRIMARY EXAMINER